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PTO/SB/21 (09-04)

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FORM**

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Total Number of Pages in This Submission

Application Number 10/574,167

Filing Date March 29, 2006

First Named Inventor BUSH et al.

Art Unit TBD

Examiner Name TBD

Attorney Docket Number 8028-007-US

ENCLOSURES (Check all that apply)

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Firm Name	CATALYST LAW GROUP, APC		
Signature			
Printed name	Michael B. Farber, Ph.D., Esq.		
Date	June 8, 2006	Reg. No.	32,612

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PATENT
8028-007-US

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)	Examiner: To Be Assigned
)	
Bush et al.)	Group Art Unit: To Be Assigned
)	
Serial No.: 10/547,176)	Docket No.: 8028-007-US
)	
Filed: March 29, 2006)	Date Mailed: June 8, 2006
)	
For: USE OF CELL LINES TO)	
PRODUCE ACTIVE THERAPEUTIC)	
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Dear Sir:

This document is an Information Disclosure Statement to the above-cited patent application.

Attached is at least one form PTO/SB/08A/B listing documents believed relevant to the subject application. The submission of the following information is not intended, nor should it be construed, to constitute an admission that any patent, article, or other information referred to herein is "prior art" unless specifically designated as such. In accordance with 37 C.F.R. § 1.97(b), the filing of this information shall not be construed to mean that a search has been made or that no other material information may exist. Neither should its submission be construed to indicate that a thorough search should not be conducted by the Examiner.

It is believed that this disclosure complies with the requirements of 37 C.F.R. § 1.96, § 1.97, and § 1.98 and the Manual of Patent Examining Procedures § 707.05(b). If for some reason the Examiner considers otherwise, it is respectfully requested that the undersigned be telephoned at (858) 450-0099 x302 so that any deficiencies can be remedied.

This Information Disclosure Statement is being submitted within three months of the filing date of the above-identified patent application. Accordingly, no fee is due for the filing of this Information Disclosure Statement under 37 C.F.R. § 1.97(b)(1).

A copy of each document is enclosed, except for issued United States patents and published United States patent applications pursuant to 37 C.F.R. § 1.98(a)(2)(ii). Some of the documents may have markings thereon. No significance is to be attached to the markings. These documents are not necessarily analogous art. Additionally, the order of the following documents is to be accorded no particular import, as the order thereof is completely fortuitous.

It is respectfully requested that these documents be: (1) fully considered by the Patent and Trademark Office during the prosecution of this application; and (2) represented on any patent which may issue on the application. Applicant respectfully requests that copies of the forms PTO/SB/08A/B, as considered and initialed by the Examiner, be returned with the next communication.

U.S. Patent No. 5,665,589 to Harris et al., issued on September 9, 1997.

U.S. Patent No. 6,046,050 to Strauss et al., issued on April 4, 2000.

U.S. Patent No. 6,107,043 to Jauregui et al., issued on August 22, 2000.

U.S. Patent No. 6,517,830 to Lollar et al., issued on February 11, 2003.

U.S. Patent No. 6,806,351 to Ruben et al. issued on October 19, 2004.

U.S. Patent Application Publication No. 2002/0045262 by Prachumsri, published on April 18, 2002.

PCT Patent Application Publication No. WO 99/55853 by Fukaya et al., published on November 4, 1999, which describes a novel immortalized hepatic cell line originating in normal human (preferably human fetal) cells, a process for producing this cell line; a method for screening compounds or salts thereof capable of inhibiting or promoting the activity of an enzyme participating in the metabolism of a biological foreign matter in the liver, inhibiting or promoting the expression of a gene encoding an enzyme participating in the metabolism of a biological foreign matter in the liver, or inhibiting or promoting the induction of the expression of a gene encoding an enzyme participating in the metabolism of a biological foreign matter in the liver, the process involving using the above-mentioned cell line. The application further describes compounds capable of inhibiting or promoting the activity of an enzyme participating in the metabolism of a biological foreign matter in the liver, compounds capable of

inhibiting or promoting the expression of a gene encoding an enzyme participating in the metabolism of a biological foreign matter in the liver, compounds capable of inhibiting or promoting the induction of the expression of a gene encoding an enzyme participating in the metabolism of a biological foreign matter in the liver, or salts of these compounds obtained by the above screening method. The cell line is described as useful in, for example, screening compounds having preventive/therapeutic effects on liver failure.

A publication, J.B. Mills et al., "Induction of Drug Metabolism Enzymes and MDR1 Using a Novel Human Hepatocyte Cell Line," J. Pharm. Exp. Therap. 309: 303-309 (2003).

A publication, B.K. Lucas et al., "High-Level Production of Recombinant Proteins in CHO Cells Using a Dicistronic DHFR Intron Expression Vector," Nucleic Acids Res. 24: 1774-1779 (1996).

A publication, U. Janssen et al., "Expression of Inter- α -Trypsin Inhibitor and Tumor Necrosis Factor-Stimulated Gene 6 in Renal Proximal Tubular Epithelial Cells," Kidney Int'l 60: 126-136 (2001).

A publication, J. Collinge et al., "Molecular Analysis of Prion Strain Variation and the Aetiology of "New Variant" CJD," Nature 383: 685-690 (1996).

A publication, C.G. White et al., "Recombinant Factor IX," Thromb. Haemost. 78: 261-265 (1997).

A publication, J.M. Soucie et al., "Hemophilia Occurrence in the United States," Am. J. Hematol. 59: 288-294 (1998).

A publication, J.P. Salier et al., "The Inter- α -Inhibitor Family: From Structure to Regulation," Biochem. J. 351: 1-9 (1996).

A publication, J. Ludlow, "Interactions Between SV40 Large-Tumor Antigen and the Growth Suppressor Proteins pRB and p53," *FASEB J.* 7: 866-871 (1993).

A publication, M. Popovic et al., "Transformation of Human Umbilical Cord Blood T-Cells by Human T-Cell Leukemia/Lymphoma Virus (HTLV)," *Proc. Natl. Acad. Sci. USA* 80:5402-5406 (1983).

A publication, A.S. Nies & S.P. Spielberg, "Principles of Therapeutics" in J.G. Hardman & L.E. Limbird, eds., "Goodman & Gilman's The Pharmacological Basis of Therapeutics" (9th ed., McGraw-Hill, New York, 1996), ch. 3., pp. 43-62.

A publication, Zola et al., in *Monoclonal Hybridoma Antibodies: Techniques and Applications* (Hurell, ed., CRC Press, 1982), pp. 51-52.

A publication, J. Rousseaux et al., "Optimal Conditions for the Preparation of Proteolytic Fragments from Monoclonal IgG of Different Rat IgG Subclasses" *Methods Enzymol.*, 121:663-69 (1986).

A publication, M. K. Paterson, "Measurement of Growth and Viability of Cells in Culture" *Methods Enzymol.* 58:141 (1979).

A publication, L.H. Thompson, "Mutant Isolation" *Methods Enzymol.* 58: 308 (1979).

A publication, Grynkiewicz et al, "A New Generation of Ca²⁺ Indicators with Greatly Improved Fluorescence Properties" *J. Biol. Chem.* 260:3440-3450 (1985).

A publication, T. Tsurimoto et al, "Stable Expression and Replication of Hepatitis B Virus Genome in an Integrated State," *Proc. Natl. Acad. Sci. USA* 84:444-448 (1987).

A publication, Y.P. Lim et al., "Correlation Between Mortality and the Levels of Inter-alpha Inhibitors in Plasma of Severely Septic Patients," J. Infect. Dis. 188:919-926 (2003).

A publication, R. Levy et al., Metabolic Drug Interactions (Lippincott, William & Wilkins, Philadelphia, PA, 2000), pp. 3-19, 51-214.

A publication, T.D. Bjorsson et al., "The Conduct of in Vitro and in Vivo Drug-Drug Interaction Studies: A PhRMA Perspective," J. Clin. Pharmacol. 43: 443-469 (2003).

A publication, A. Madan et al., "Effects of Prototypical Microsomal Enzyme Inducers on Cytochrome P450 Expression in Cultured Human Hepatocytes," Drug Metab. Dispos. 31: 421-431 (2003).

A publication, E. LeCluyse et al., "Cultured Rat Hepatocytes" in Models for Assessing Drug Absorption and Metabolism (R.T. Borchard et al., eds., P.L Smith & G. Wilson, Plenum Press, New York, 1996), ch. 9., pp. 121-160.

A publication, E. LeCluyse et al., "Strategies for Restoration and Maintenance of Normal Hepatic Structure and Function in Long-Term Cultures of Rat Hepatocytes," Adv. Drug Delivery Rev. 22: 133-186 (1996).

A publication, D. Mudra & A. Parkinson, "Preparation of Hepatocytes for Drug Metabolism Studies" in Current Protocols in Toxicology Unit 5.8. (M Maines et al., eds., John Wiley & Sons, Inc. 2001), Unit 5.8.

A publication, A. Madan et al., "Effect of Cryopreservation on Cytochrome P450 Enzyme Induction in Cultured Rat Hepatocytes," Drug Metab. Dispos. 27: 327-335 (1999).

A publication, E. LeCluyse et al., "Influence of Extracellular Matrix Overlay and Medium Formulation on the Induction of Cytochrome P450 2B in Primary Cultures of Rat Hepatocytes," *Drug Metab. Dispos.* 27: 909-915 (1999).

A publication, E. LeCluyse et al., "Expression and Regulation of Cytochrome P450 Enzymes in Primary Cultures of Human Hepatocytes," *J. Biochem. Mol. Toxicol.* 14: 177-188 (2000).

A publication, Luo et al., "CYP3A4 Induction by Drugs: Correlation Between a Pregnane X Receptor Reporter Gene Assay and CYP3A4 Expression in Human Hepatocytes," *Drug Metab. Dispos.* 30: 795-804 (2002).

A publication, A. Abid et al., "Expression and Inducibility of UDPglucuronyltransferases by 1-Naphthol in Human Cultured Hepatocytes and Hepatocarcinoma Cell Lines," *Life Sci.* 60: 1943-1951 (1997).

A publication, A.M. Baciewicz et al., "Update on Rifampin Drug Interactions," *Arch. Intern. Med.* 147: 565-568 (1987).

A publication, G. Bertilsson et al., (1998) "Identification of a Human Nuclear Receptor Defines a New Signaling Pathway for CYP3A Induction," *Proc. Natl. Acad. Sci. USA* 95: 12208-12213 (1998).

A publication, M.D. Burke et al., "Ethoxy-, Pentoxy- and Benzyloxyphenoxazones and Homologues: A Series of Substrates to Distinguish Between Different Induced Cytochromes P-450," *Biochem. Pharmacol.* 34: 3337-3345 (1985).

A publication, P.S. Eis et al., "An Invasive Cleavage Assay for Direct Quantitation of Specific RNAs," *Nature Biotechnol.* 19: 673-676 (2001).

A publication, S.S. Ferguson et al., "Regulation of Human CYP2C9 by the Constitutive Androstane Receptor: Discovery of a New Distal Binding Site," *Mol. Pharmacol.* 62: 737-746 (2002).

A publication, A. Geick et al., "Nuclear Receptor Response Elements Mediate Induction of Intestinal MDR1 by Rifampin," *J. Biol. Chem.* 276: 14581-14587 (2001).

A publication, T. Leemann et al., "Cytochrome P450TB (CYP2C): A Major Monooxygenase Catalyzing Diclofenac 4'-Hydroxylation in Human Liver," *Life Sci.* 52: 29-34 (1993).

A publication, J.M. Lehmann et al. "The Human Orphan Nuclear Receptor PXR is Activated by Compounds that Regulate CYP3A4 Gene Expression and Cause Drug Interactions," *J. Clin. Invest.* 102: 1016-1023 (1998).

A publication, A.P. Li et al., "Primary Human Hepatocytes as a Tool for the Evaluation of Structure-Activity Relationship in Cytochrome P450 Induction Potential of Xenobiotics: Evaluation of Rifampin, Rifapentine and Rifabutin," *Chem. Biol. Interact.* 107: 17-30 (1997).

A publication, W. Li et al., "Regulation of Cytochrome P450 Enzymes by Aryl Hydrocarbon Receptor in Human Cells," *Biochem. Pharmacol.* 56: 599-612 (1998).

J.M Pascussi et al., "The Expression of CYP2B6, CYP2C9 and CYP3A4 Genes: A Tangle of Networks of Nuclear and Steroid Receptors," *Biochim. Biophys. Acta* 1619: 243-253 (2003).

A publication, A.D. Rodrigues & R.A. Prough RA, "Induction of Cytochromes P450IA1 and P450IA2 and Measurement of Catalytic Activities," *Methods Enzymol.* 206: 423-431 (1991).

A publication, J. Sahi et al., "Avasimibe Induces CYP3A4 and Multiple Drug Resistance Protein 1 Gene Expression Through Activation of the Pregnane X Receptor," J. Pharmacol. Exp. Ther. 306: 1027-1034 (2003).

A publication, E.G. Schuetz et al., "Modulators and Substrates of P-Glycoprotein and Cytochrome P4503A Coordinately Up-Regulate These Proteins in Human Colon Carcinoma Cells," Mol. Pharmacol. (49): 311-318 (1996).

A publication, A.J. Sonderfan et al., "Regulation of Testosterone Hydroxylation by Rat Liver Microsomal Cytochrome P-450," Arch. Biochem. Biophys. 255: 27-41 (1987).

A publication, A.J. Sonderfan & A. Parkinson, "Inhibition of Steroid 5 Alpha-Reductase and Its Effects on Testosterone Hydroxylation by Rat Liver Microsomal Cytochrome P-450," Arch. Biochem. Biophys. 265: 208-218 (1988).

A publication, E. Spina et al., "Clinically Significant Pharmacokinetic Drug Interactions with Carbamazepine: An Update," Clin. Pharmacokinet. 31: 198-214 (1996).

A publication, R.G. Tirona et al., "Human Organic Anion Transporting Polypeptide-C (SLC21A6) Is a Major Determinant of Rifampin-Mediated Pregnane X Receptor Activation," J. Pharmacol. Exp. Ther. 304: 223-228 (2003).

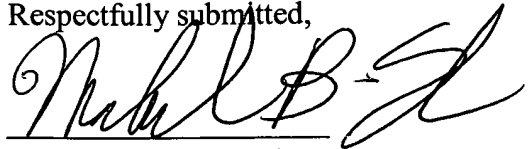
A publication, J.P. Whitlock et al., "Induction of Cytochrome P4501A1: A Model for Analyzing Mammalian Gene Transcription," FASEB 10: 809-818 (1996).

A publication, A.J. Williams et al., "Comparative Metabolic Capabilities of CYP3A4, CYP3A5, and CYP3A7," Drug Metab. Dispos. 30: 883-891(2002).

A publication, A.W. Wood et al., "Regio- and Stereoselective Metabolism of two C19 Steroids by Five Highly Purified and Reconstituted Rat Hepatic Cytochrome P-450 Isozymes," J. Biol. Chem. 258: 8839-8847 (1983).

Date: June 8, 2006

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Michael B. Farber', written over a horizontal line.

Michael B. Farber, Ph.D., Esq.
Reg. No.: 32,612

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Complete if Known

Application Number	10/574 167
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Filing Date	March 29, 2006
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First Named Inventor	BUSH et al.
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Art Unit	TBD
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Examiner Name	TBD
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Attorney Docket Number	8028-007-US
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U. S. PATENT DOCUMENTS

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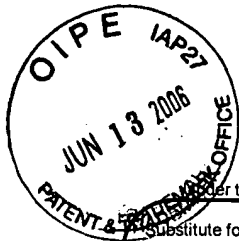
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		J.B. MILLS et al., "Induction of Drug Metabolism Enzymes and MDR1 Using a Novel Human Hepatocyte Cell Line," J. Pharm. Exp. Therap. 309: 303-309 (2003).	
		B.K. LUCAS et al., "High-Level Production of Recombinant Proteins in CHO Cells Using a Dicistronic DHFR Intron Expression Vector," Nucleic Acids Res. 24: 1774-1779 (1996).	
		U. JANSSEN et al., "Expression of Inter- α -Trypsin Inhibitor and Tumor Necrosis Factor-Stimulated Gene 6 in Renal Proximal Tubular...", Kidney Int'l 60: 126-136 (2001).	
		J. COLLINGE et al., "Molecular Analysis of Prion Strain Variation and the Aetiology of "New Variant" CJD," Nature 383: 685-690 (1996).	
		C.G. WHITE et al., "Recombinant Factor IX," Thromb. Haemost. 78: 261-265 (1997).	
		J.M. SOURCIE et al., "Hemophilia Occurrence in the United States," Am. J. Hematol. 59: 288-294 (1998).	
		J.P. SALIER et al., "The Inter- α -Inhibitor Family: From Structure to Regulation," Biochem. J. 351: 1-9 (1996).	
		J. LUDLOW, "Interactions Between SV40 Large-Tumor Antigen and the Growth Suppressor Proteins pRB and p53," FASEB J. 7: 866-871 (1993).	
		M. POPOVIC et al., "Transformation of Human Umbilical Cord Blood T-Cells by Human T-Cell Leukemia/Lymphoma Virus (HTLV)," Proc. Natl. Acad. Sci. USA 80:5402-5406 (1983).	
		A.S. NIES & S.P. SPIELBERG, "Principles of Therapeutics" in J.G. Hardman & L.E. Limbird, eds., "Goodman &...", (9th ed., McGraw-Hill, New York, 1996), ch. 3., pp. 43-62.	

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		Application Number	10/574,167		
		Filing Date	March 29, 2006		
		First Named Inventor	BUSH et al.		
		Art Unit	TBD		
		Examiner Name	TBD		
Sheet	2	of	5	Attorney Docket Number	8028-007-US

NON PATENT LITERATURE DOCUMENTS			
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		ZOLA et al., in Monoclonal Hybridoma Antibodies: Techniques and Applications (Hurell, ed., CRC Press, 1982), pp. 51-52.	
		J. ROUSSEAU et al., "Optimal Conditions for the Preparation of Proteolytic Fragments from Monoclonal IgG of Different Rat IgG Subclasses" Methods Enzymol., 121:663-69 (1986).	
		M. K. PATERSON, "Measurement of Growth and Viability of Cells in Culture" Methods Enzymol. 58:141 (1979).	
		L.H. THOMPSON, "Mutant Isolation" Methods Enzymol. 58: 308 (1979).	
		GRYNKIEWICZ et al, "A New Generation of Ca ²⁺ Indicators with Greatly Improved Fluorescence Properties" J. Biol. Chem. 260:3440-3450 (1985).	
		T. TSURIMOTO et al, "Stable Expression and Replication of Hepatitis B Virus Genome in an Integrated State," Proc. Natl. Acad. Sci. USA 84:444-448 (1987).	
		Y.P. LIM et al., "Correlation Between Mortality and the Levels of Inter-alpha Inhibitors in Plasma of Severely Septic Patients," J. Infect. Dis. 188:919-926 (2003).	
		R. LEVY et al., Metabolic Drug Interactions (Lippincott, William & Wilkins, Philadelphia, PA, 2000), pp. 3-19, 51-214.	
		T.D. BJORSSON et al., "The Conduct of in Vitro and in Vivo Drug-Drug Interaction Studies: A PhRMA Perspective," J. Clin. Pharmacol. 43: 443-469 (2003).	
		A. MADAN et al., "Effects of Prototypical Microsomal Enzyme Inducers on Cytochrome P450 Expression in Cultured Human Hepatocytes," Drug Metab. Dispos. 31: 421-431 (2003).	

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		E. LECLUYSE et al., "Cultured Rat Hepatocytes" in Models for..., (R.T. Borchard et al., eds., P.L Smith & G. Wilson, Plenum Press, New York, 1996), ch. 9., pp. 121-160.	
		E. LECLUYSE et al., "Strategies for Restoration and Maintenance of Normal Hepatic Structure and Function in Long-Term Cultures...", Adv. Drug Delivery Rev. 22: 133-186 (1996).	
		D. MUDRA & A. PARKSINSON, "Preparation of Hepatocytes for...", in Current Protocols in Toxicology Unit 5.8. (M Maines et al., eds., John Wiley & Sons, Inc. 2001), Unit 5.8.	
		A. MADAN et al., "Effect of Cryopreservation on Cytochrome P450 Enzyme Induction in Cultured Rat Hepatocytes," Drug Metab. Dispos. 27: 327-335 (1999).	
		E. LECLUYSE et al., "Influence of Extracellular Matrix Overlay and Medium Formulation on the Induction of Cytochrome P450 2B in...", Drug Metab. Dispos. 27: 909-915 (1999).	
		E. LECLUYSE et al., "Expression and Regulation of Cytochrome P450 Enzymes in Primary Cultures of Human Hepatocytes," J. Biochem. Mol. Toxicol. 14: 177-188 (2000).	
		LUO et al., "CYP3A4 Induction by Drugs: Correlation Between a Pregnane X Receptor Reporter Gene Assay and CYP3A4...", Drug Metab. Dispos. 30: 795-804 (2002).	
		A. ABID et al., "Expression and Inducibility of UDPglucuronyltransferases by 1-Naphthol in Human Cultured Hepatocytes and Hepatocarcinoma...", Life Sci. 60: 1943-1951 (1997).	
		A.M. BACIEWICZ et al., "Update on Rifampin Drug Interactions," Arch. Intern. Med. 147: 565-568 (1987).	
		G. BERTILSSON et al., (1998) "Identification of a Human Nuclear Receptor Defines a New Signaling Pathway for CYP3A...", Proc. Natl. Acad. Sci. USA 95: 12208-12213 (1998).	

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		M.D. BURKE et al., "Ethoxy-, Pentoxy- and Benzyloxyphenoxazones and Homologues: A Series of Substrates to Distinguish Between...", Biochem. Pharmacol. 34: 3337-3345 (1985).	
		P.S. EIS et al., "An Invasive Cleavage Assay for Direct Quantitation of Specific RNAs," Nature Biotechnol. 19: 673-676 (2001).	
		S.S. FERGUSON et al., "Regulation of Human CYP2C9 by the Constitutive Androstane Receptor: Discovery of a New Distal Binding Site," Mol. Pharmacol. 62: 737-746 (2002).	
		A. GEICK et al., "Nuclear Receptor Response Elements Mediate Induction of Intestinal MDR1 by Rifampin," J. Biol. Chem. 276: 14581-14587 (2001).	
		T. LEEMANN et al., "Cytochrome P450TB (CYP2C): A Major Monooxygenase Catalyzing Diclofenac 4'-Hydroxylation in Human Liver," Life Sci. 52: 29-34 (1993).	
		J.M. LEHMANN et al. "The Human Orphan Nuclear Receptor PXR is Activated by Compounds that Regulate CYP3A4 Gene Expression and...", J. Clin. Invest. 102: 1016-1023 (1998).	
		A.P. LI et al., "Primary Human Hepatocytes as a Tool for the Evaluation of Structure-Activity Relationship in Cytochrome P450...", Chem. Biol. Interact. 107: 17-30 (1997).	
		W. LI et al., "Regulation of Cytochrome P450 Enzymes by Aryl Hydrocarbon Receptor in Human Cells," Biochem. Pharmacol. 56: 599-612 (1998).	
		J.M. PASCUSI et al., "The Expression of CYP2B6, CYP2C9 and CYP3A4 Genes: A Tangle of Networks of Nuclear and Steroid Receptors," Biochim. Biophys. Acta 1619: 243-253 (2003).	
		A.D. RODRIGUES & R.A. PROUGH RA, "Induction of Cytochromes P450IA1 and P450IA2 and Measurement of Catalytic Activities," Methods Enzymol. 206: 423-431 (1991).	

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		E.G. SCHUETZ et al., "Modulators and Substrates of P-Glycoprotein and Cytochrome P4503A Coordinately Up-Regulate These Proteins...", Mol. Pharmacol. (49): 311-318 (1996).	
		A.J. SONDERFAN et al., "Regulation of Testosterone Hydroxylation by Rat Liver Microsomal Cytochrome P-450," Arch. Biochem. Biophys. 255: 27-41 (1987).	
		A.J. SONDERFAN & A. PARKINSON, "Inhibition of Steroid 5 Alpha-Reductase and Its Effects on Testosterone Hydroxylation by Rat...", Biochem. Biophys. 265: 208-218 (1988).	
		E. SPINA et al., "Clinically Significant Pharmacokinetic Drug Interactions with Carbamazepine: An Update," Clin. Pharmacokinet. 31: 198-214 (1996).	
		R.G. TIRONA et al., "Human Organic Anion Transporting Polypeptide-C (SLC21A6) Is a Major Determinant of Rifampin-Mediated...", J. Pharmacol. Exp. Ther. 304: 223-228 (2003).	
		J.P. WHITLOCK et al., "Induction of Cytochrome P4501A1: A Model for Analyzing Mammalian Gene Transcription," FASEB 10: 809-818 (1996).	
		A.J. WILLIAMS et al., "Comparative Metabolic Capabilities of CYP3A4, CYP3A5, and CYP3A7," Drug Metab. Dispos. 30: 883-891(2002).	
		A.W. Wood et al., "Regio- and Stereoselective Metabolism of two C19 Steroids by Five Highly Purified and Reconstituted Rat...", J. Biol. Chem. 258: 8839-8847 (1983).	

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